Depression is a Precursor or Resultant Factor of Coronary Heart Disease

Ashima Mandla, IInd Year

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Both Coronary Heart Disease and Depression are categorized as 'non-communicable diseases'. Nowadays, they are being referred as 'lifestyle diseases' because they are largely dependent on the kind of lifestyle an individual maintains.

CORONARY HEART DISEASE (CHD)

Coronary artery disease is "narrowing of the lumen of one or more of the coronary arteries, usually due to atherosclerosis; myocardial ischemia; can cause congestive heart failure, angina pectoris, or myocardial infarction. CHD is a narrowing of the small blood vessels that supply blood and oxygen to the heart. It is also known as *Coronary Artery Disease.* Coronary heart disease is generally caused by *atherosclerosis* - when plaque (cholesterol substances) accumulates on the artery walls, causing them to narrow. *Ischaemic or ischemic heart disease* (IHD), *or myocardial ischaemia*, a disease characterized by ischaemia (reduced blood supply) of the heart muscle, can also cause it. It commonly causes *angina pectoris* (chest pain), shortness of breath, heart attack (*myocardial infarction*), *congestive heart failure* and other symptoms. The coronary arteries bring blood and oxygen to your heart and thus play an integral role in the normal functioning of the heart.

Atherosclerosis (also known as arteriosclerotic vascular disease or ASVD) is a condition in which an artery wall thickens as a result of the accumulation of fatty materials such as cholesterol. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, caused largely by the accumulation of macrophage white blood cells and promoted by low-density lipoproteins (plasma proteins that carry cholesterol and triglycerides) without adequate removal of fats and cholesterol from the macrophages by functional high-density lipoproteins (HDL).

Myocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack, is the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction

in blood supply) and oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (infarction) of heart muscle tissue (myocardium).

The factors underlying CHD can be divided into mainly two categories:

1. Factors that CANNOT be controlled by an individual.
2. Factors that CAN be controlled by an individual.

The risk factors for coronary heart disease that you CANNOT change are:

- Age – Research has shown that the risk of heart disease increases with age.
- Gender - Men have a higher risk of getting heart disease than women who are still getting their menstrual period. After menopause, the risk for women is closer to the risk for men.
- Genetic component - If your parents or other close relatives had suffered from heart disease, you are at higher risk as research suggests. However, the importance of genetic factors in the majority of the cases is largely unknown.
- Race – Research has also shown that one's race can also affect CHD. African Americans, Mexican Americans, American Indians, Hawaiians, and some Asian Americans also have a higher risk for heart problems.
- Personality – Type A personality (Friedman and Rosenman) is associated with competitive drive, restlessness, hostility and a sense of urgency or impatience. Type A personality individuals are more prone to coronary heart disease, hypertension. The risk of developing CHD with Type-A is sometimes greater than the risks caused by smoking, hypertension and elevated serum cholesterol levels.

The lifestyle related risk factors for coronary heart disease:

- Diabetes mellitus- the risk of CHD is 2-3 times higher in diabetics than in non-diabetics. CHD is responsible for 30 to 50 percent of deaths in diabetics over the age of 40 in industrialized countries.
- Hypertension- it accelerates the atherosclerotic process (fatty depositions inside the arterial walls), especially if hyperlipidemia(high cholesterol) is present.
- Serum Cholesterol: Low levels of HDL-C Cholesterol, high levels of LDL block the arteries, which can result in CHD. Vast body of evidence has shown a triangular relationship between habitual diet, cholesterol-lipoprotein and CHD.
- Substance abuse- is an independent risk factor for CHD. In terms of alcohol intake, 75g or more per day can lead to CHD. Whereas in terms of smoking, carbon monoxide

induced atherogenesis, nicotine stimulation of adregenic drives raising blood pressure and myocardial oxygen demand can together lead to CHD.

- Vascular Diseases - People with narrowed arteries in another part of the body (examples are stroke and poor blood flow to the legs) are more prone to CHD.

- Being overweight- sedentary life-style is associated with a greater risk of development of early CHD. There is evidence that regular physical exercise increases concentration of HDL and decreases body weight and blood pressure, which are beneficial for cardiovascular health.

- High levels of stress and Depressive tendencies - The incidence of heart attacks and sudden death have been shown to increase significantly following the acute stress of natural disasters like hurricanes, earthquakes and tsunamis and as a consequence of any severe stressor that evokes "fight or flight' responses. Coronary heart disease is also much more common in individuals subjected to chronic stress and recent research has focused on how to identify and prevent this growing problem, particularly with respect to job stress. In many instances, we create our own stress that contributes to coronary disease by smoking and other faulty lifestyles or because of dangerous traits like excess anger, hostility, aggressiveness, time urgency, inappropriate competitiveness and preoccupation with work. The relationship between stress and depression and either of them with CHD is complicated. As per research it is still difficult to determine whether stress or/ and depression lead to CHD or it is the other way round.

Depression

DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) classifies depression into mood disorders. Mood disorders can be defined as psychological disorders in which individuals experience swings in their emotional states that are much more extreme and prolonged than is true of most people.

Causes of Depression:

Biological causes: Neurotransmitters

Within the brain, there are special chemicals called neurotransmitters that carry out many very important functions. Essentially, they help transfer messages throughout structures of the brain's nerve cells. Of the 30 or so neurotransmitters that have been identified, researchers have discovered associations between clinical depression and the function of three primary ones: serotonin, norepinephrine, and dopamine. These three neurotransmitters function within structures of the brain that regulate emotions, reactions to stress, and the physical drives of sleep, appetite, and sexuality. Structures that have received a great deal of attention from depression researchers include the limbic system and hypothalamus.

Theories about how neurotransmitters may be related to a person's mood have been based upon the effects that antidepressant medications can have on relieving depression in some people. It is believed that these medications are effective because they regulate the amount of specific neurotransmitters in the brain. However, the role that neurotransmitters play in the development or treatment of clinical depression is not completely clear. For instance, it has been shown that many people who are depressed have low levels of the neurotransmitter norepinephrine. The use of some antidepressants can increase the level of norepinephrine in the brain, and subsequently relieve depressive symptoms. One the other hand, it has also been shown that some other people who are depressed have high levels of norepinephrine. This same scenario may be true for other neurotransmitters.

Another reason that the effects of neurotransmitters are not clear-cut has to do with the fact that antidepressant medications do not work for everyone. If there were a direct causal link between the level of a neurotransmitter in the brain and depression, then we would expect a much higher rate of success with medication. Further, although antidepressant medications can change the level of a neurotransmitter in the brain immediately, it normally takes a few weeks for a person with depression to feel better. What is seems to boil down to is that there appears to be a strong relationship between neurotransmitter levels in the brain and clinical depression, and that antidepressant medications work for a great many people, but we are not absolutely certain of the actual relationship between neurotransmitters and depression.

The reason we do not know more about the effects of neurotransmitters has to do with that fact that they are so difficult to study. Neurotransmitters are present in very small quantities, they are only available in certain locations within the brain, and they disappear very quickly once they are used. Researchers can only measure what is left over after their use in the brain. The substances that remain are called metabolites and they can be found in blood, urine, and cerebrospinal fluid. By measuring these metabolites, researchers can gain an understanding of the effects of changes in neurotransmitters in the brain.It is unknown whether changes in levels of neurotransmitters cause the development of depression or depression causes changes in neurotransmitters. It may happen both ways. Researchers believe that our behavior can affect our brain chemistry, and that brain chemistry can affect behavior. For instance, if a person experiences numerous stressors or traumas this may cause his or her brain chemistry to be affected, leading to clinical depression. On the other hand, that same person may learn how to change depressed thoughts and behavior and cope with stressful events. Doing this may also change brain chemistry and relieve depression.

Cortisol: Of those individuals who are clinically depressed, about one-half will have an excess of a hormone in their blood called cortisol. Cortisol is secreted by the adrenal glands. Located near the kidneys, the adrenal glands assist us in our reactions to stressful events. Cortisol may continue to be secreted even though a person already has high levels in his or her blood. This hormone is believed to be related to clinical depression since the high levels usually reduce to a normal level once the depression disappears. People who are not depressed tend to have

secretions of cortisol at certain times of the day. Cortisol levels are highest at approximately 8:00 a.m. and 4:00 p.m., and then lowest during the night. This normal cycling of cortisol levels does not occur in some people who are depressed. For instance, they might have a consistent level of cortisol all the time, or highest amounts in the middle of the night.

Psychological factors: A variety of psychological factors appear to play a role in vulnerability to these severe forms of depression. Most likely, psychological factors are completely responsible for other forms of mild and moderate depression, especially reactive depression. Reactive depression is usually diagnosed as an adjustment disorder during treatment. To state them briefly, people who have low self-esteem, who consistently view themselves and the world with pessimism, or who are readily overwhelmed by stress are more prone to depression. Psychologists often describe social learning factors as being significant in the development of depression, as well as other psychological problems. People learn both adaptive and maladaptive ways of managing stress and responding to life problems within their family, educational, social and work environments.

These environmental factors influence psychological development, and the way people try to resolve problems when they occur. Social learning factors also explain why psychological problems appear to occur more often in family members, from generation to generation. If a child grows up in a pessimistic environment, in which discouragement is common and encouragement is rare, that child will develop a vulnerability to depression as well. A serious loss, chronic illness, relationship problems, work stress, family crisis, financial setback, or any unwelcome life change can trigger a depressive episode. Very often, a combination of biological, psychological, and environmental factors are involved in the development of depressive disorders, as well as other psychological problems.

Depression is very common and is in fact experienced by 21.3 percent of women and 12.7 percent of men at some time during their lives (Kessler et al, 1994). This nearly two-to-one gender difference in depression rates has been reported in many studies (Culberton, 1997) especially in studies conducted in wealthy, developed countries. Gender differences may also stem, at least to a degree, from the fact that females are more willing to admit to such feelings than males, or from the fact that women are more likely to remember such episodes (Wilhelm & Parker, 1994). Individual also suffer from double depression in which they recover from major depression but continue to experience a depressed mood (dysthymic disorder) or some cases, unusual irritability.

THEORIES AND RESEARCHES

Glassman and Shapiro suggested that the impact of depression on cardiac mortality depends on baseline cardiac disease status because the risk of cardiac events that depression confers seems to be smaller in subjects with cardiac disease status than with cardiac disease status.

Macrophage Theory of Depression (Smith,1991): suggests that excessive secretion of macrophage monokines is proposed as the cause of depression. Monokines when given to volunteers can produce the symptoms necessary for the Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised (DSM-III-R) diagnosis of major depressive episode. Interleukin-1 (IL-1) can provoke the hormone abnormalities linked with depression. This theory provides an explanation for the significant association of depression with coronary heart disease, rheumatoid arthritis, stroke and other diseases where macrophage activation occurs. The 3:1 female/male incidence of depression ratio is accounted for by estrogen's ability to activate macrophages. The extraordinary low rate of depression in Japan is consistent with the suppressive effect of eicosapentanoic acid on macrophages. Fish oil is proposed as a prophylaxis against depression and omega-6 fat as a promoter. Infection, tissue damage, respiratory allergies and antigens found in food are some of the possible causes of macrophage activation triggering depression.

There are many factors contributing to the development and progression of CHD: smoking, dislipidemia or hyperlipidemia, hypertension, diabetes mellitus and age (Grundy et al, 1998). Current research suggests the role of psychosocial factors contributing to CHD, specifically depression (Frasure-Smith et al, 1995 a).

The link between depression and CHD is well documented and has indicated depression is predictive of developing CHD in initially healthy individuals (Aaroma et al. 1995, Barefoot and Schroll 1996, Pratt et al. 1996, Ford et al. 1998, Mendes de Leon et al. 1998, Whooley and Browner 1998, Ferketich et al. 2000) as well as predictive of secondary cardiac event and mortality in cardiac patients (Frasure-Smith et al. 1995a, 1995b;Lesperanceetal. 1996; Frasure-Smith et al. 1999; Lesperance et al. 2000; Lesperance et al. 2002). Depression appears to increase the risk of CHD through both physiological mechanisms and behavior patterns (for a review, see Rozanski et al. 1999). Depressed CHD patients also appear to be at direct physiological risk for future cardiac events via autonomie dysregulation through hyperactivity of the pituitary gland (Carney et al. 1995, Mussel man et al. 1998, Carney et al. 2002), reduced heart rate variability and increased heart rate (Carney et al., 1995, Carney et al. 2000, Gorman and Sloan ,2000; Stein et al. 2000, Carney et al. 2002), inflammatory processes (Miller et al. 2003), platelet function (Glassman and Shapiro 1998,Musselman et al. 1998, Feng et al. 1999, Lederbogen et al. 2001), and immune response (Ladwig et al. 2003, Miller et al.2003, Lesperance et al. 2004).

Depression may place CHD patients at greater risk indirectly through unhealthy behavior patterns: cigarette smoking (Barefoot and Schroll 1996, Ford et al. 1998, Mayou et al. 2000, Brummett et al. 2003), decreased physical activity (Mayou et al. 2000, Brummett et al. 2003), poor diet (Mayou et al. 2000, Ziegelstsein et al. 2000), and medical adherence problems (Carney et al. 1995, Ziegelstein et al. 2000, Romanelli et al. 2002, Wang et al. 2002), all of which have been found to be associated with depression. Major depression occurs in 15 to 20 % of

hospitalized CHD patients with some 30 to 50% demonstrating at least some depression symptoms(Lesperance & Frasure-Smith, 2000).

Different sets of mechanism may link CHD and depression at different points in the disease process. Decreased heart rate variability is one of the mechanisms by which depression may lead to cardiac events. There is evidence that the beat-to-beat variation in heart rate is reduced in depression (Carney et al., 2001). Decreased heart rate variability is thought to reflect increased sympathetic tone, decreased vagal (parasympathetic nervous system) activity or both. Post myocardial infarction patients, people with congestive heart failure, and diabetics all have reduced heart rate variability, and the greater the reduction in variability, the worse their prognosis. Depressed patients with CHD tend to have even more pronounced decreases in heart rate variability than non-depressed CHD patients. Thus, changes in heart rate variability may at least partially account for depression's negative association with cardiac prognosis. Although it is also possible that depression and its physiological sequences are not the cause of cardiac disease, but rather its consequences; the evidence for this mechanism is not very strong.

Indices of cardiac severity, such as poor pumping function and the number of blocked coronary arteries, are moderately associated with the level of depressive symptoms, depression's association with cardiac prognosis is statistically independent of these factors.

Models discussing the link between Depression and CHD :-

Vascular depression hypothesis of depression suggests that in advances atherosclerosis, blockages in the brain arteries may compromise blood function of nerve cells in brain regions involved in mood and cognition, leading to depression (Alexopoulos et al., 1997). Similarly, atherosclerotic blockages in coronary arteries produce CHD. Thus, the link between depression and CHD, at least in elderly, may be the result of generalized atherosclerosis. The cytokine model of depression focuses on the inflammatory nature of the atherosclerotic process (Danztzer, Wollman & Yirmiya, 2002). The buildup of cholesterol and other substances in the linings of the arteries contains immune cells that produce cytokines, chemicals that orchestrate the inflammatory response and have widespread systematic effects. Cytokines can produce, what is called sickness behavior, which includes loss of appetite and interest, fatigue, and social withdrawal; these behaviors being closely related to depression. It is well established that increased levels of inflammatory markers predict worsening of cardiac prognosis, these patterns are similar in patients with depression.

A relative deficiency in the polyunsaturated omega-3 free fatty acids, found primarily in fatty fish is associated with an increased risk of CHD, as well as with depression (Frasure-Smith & Julien, 2004). Research has shown that the more fish in the average diet, the lower the incidence of CHD. Also, omega-3 supplementation may have anti-depressant properties. Thus a deficiency of polyunsaturated omega—3 free fatty acids could be a risk factor for both CHD and depression, and a diet rich in omega-3 could be beneficial for both conditions.

Changes in blood clotting may also be a mechanism linking depression and CHD. Both myocardial infarction and unstable angina involve the formation of a blood clot within the arteries of the heart. This process if often triggered by the rupture of the atherosclerotic plaque, which releases material that activates the blood platelets. Platelets contain serotonin and have the capacity to secrete, respond to and reabsorb serotonin. One of the antidepressants, the selective serotonin reuptake inhibitors (SSRI's), is thought to affect depression by decreasing the re-absorption of serotonins into platelets, thereby decreasing its availability. Studies suggest that heightened platelet activation and propensity to form blood clots are associated with depression, and some evidence that SSRI's may decrease platelet activation. A genetic predisposition to serotonin dysfunction in the brain that leads to depression, can also independently lead to increased platelet activation and coronary events.

One line of research examining depression and CHD has taken place in cardiac rehabilitation (CR). Cardiac rehabilitation consists of three phases:

- Phase I CR is the inpatient phase, emphasizing patient education about healthy behaviors and emotional stress reduction (Ku et' al 2002).

- Phase II CR is an outpatient phase consisting of three 60 minute exercise sessions per week with electro cardiograph (ECG) monitoring for a maximum of 12 weeks (Paul-Labrador et'al. 1999). This phase is typically covered by medical insurance(Centers for Medicare and Medicaid, 2002)

- Phase III CR consists of some supervision with little or no ECG monitoring (Balady et al. 2000). This phase is typically not covered by medical insurance and thus results in a out-of-pocket- pay.

- Phase IV CR is considered the maintenance phase and continues throughout life (Watson, 2002). This phase consists of ECG monitoring at intervals and little supervision from the doctors. No coverage is given by medical insurance and a patient in this stage requires to pay the cost for the follow-up treatment.

Depression in CR patients is typically dependent the patient's desire to continue the struggle to maintain themselves in order to live and thus adhere to the physician and psychiatrist or psychologists' recommendation. Virtually all of the research on depression in CR patients has been performed on Phase II CR patients (Milani et al 1996, Yoshida et al 1999, Zeigelstein et al 2000 and so on). Very little research has been performed on Phase III/IV patients and the research performed has not examined differences in depression scores between Phase II and Phase III/IV CR patients (Turner et al 2002)

Research Studies: Donoho, Stalls, Sydeman (2011), in an original article, used the Beck Depression Inventory(BDI)on patients of phases II, III and IV. The purpose of this study was to determine whether there is a difference in the levels of depression in individuals in Phase II and

III/IV as previous research concentrated on only phase II patients. The authors of this article speculated that the lack of research on depression and CHD in Phase II and III/IV patients may be due to a need for an out-of-the-pocket expense in Phase III and IV resulting in people belonging to lower socio-economic background to back out. This study hypothesized that depression would be more prevalent in Phase II CR patients as compared to phase III/IV patients. BDI was used to categorize the patients as suffering for high or low depression. A score on BDI >/ 10 was categorized as high depression whereas a score /<10 was categorized as low depression. A cut score of 10 was utilized because of its common use in cardiac studies (Frasure smith et al. 1995). 32 participants from Cardiopulmonary Rehabilitation Clinic were recruited with a mean age of 64 years. The sample consisted of 72% females and predominantly Caucasians. The results indicated that Phase II and III/IV patients do not differ in prevalence of depression. Statistical analysis indicated that 4 of 12 (33%) phase II patients and 5 of 20 (25%) phase III/IV patients were high in depression.

In a study by Penninix, Aartijan et al (2001) in an original article conducted a longitudinal community based study on elderly persons from 11 districts of Netherlands. This study examined and compared the effect of significant depressive symptoms (minor depression) and major depression on cardiac mortality with an elderly sample of both with and without cardiac disease. A total of 2847 men and women aged 55 to 85 years were evaluated for 4 years. 450 out of 2847 were confirmed myocardial infarction, angina pectoris or congestive heart failure. The sample population was adjusted for smoking, alcohol use, hypertension and body mass index. The Epidemiologic depression scale (CES-D) was used to diagnose minor depression. A score of 16 was used as a cut off for diagnosing the individual as suffering from minor depression. For major depression, the criteria given in the DSM-III was used.

Thus if an individual scored 16 points or above and did not meet the criteria given by DSM-III, then it is categorized as minor depression and if both criterion is meet then it is categorized as major depression. The Cox Proportional Hazard Regression model was used and was found that the risk of cardiac mortality is higher with age, especially in males, affects individuals with lower educational backgrounds, individuals with low Body Mass Index(BMI), diabetes mellitus or any vascular diseases.

In the 50 months follow up, it was seen that depressed older persons were more likely to die irrespective of their cardiac previous condition. Thus, an increased cardiac mortality risk associated with depression was present, similar in both subjects with or without cardiac disease. For cardiac disease patients, the relative risk of subsequent cardiac mortality was 1.6 times for minor depression and 3 times for major depression (a statistical result obtained using 95% confidence). For subjects without cardiac disease, at baseline, similarly increased cardiac mortality risk found was 1.5 times for minor depression and 3.9 times for major depression. This study thus, could not find evidence strong enough to conclude that a stronger affect of depression in seen in cardiac patients vs. non-cardiac patients.

Frasure-Smith and Lesperance (2005), in a review article, stated that depression is associated with both the incidence and prognosis of CHD, in contrast to the Phennix, Aartijan et al (2001) study . They hypothesized that depression increases cardiac mortality by 2 times. They administered the Beck Depression Inventory (BDI-1987) to 896 Canadian patients, hospitalized for an acute myocardial infarction and followed them for 5 years post discharge. A significant relationship was found between the BDI scores and cardiac mortality. The increasing risk of cardiac mortality began to be apparent, in these subjects, below the usual level of symptoms considered to indicate depression (BDI>/ 10) and was independent of the severity of cardiac disease, as well as factors such as age, sex, education and marital status. As per the statistical analysis, correlation between cardiac death percentage and BDI score was as follows : scores on BDI>/ 5 with a corresponding cardiac death percentage of 7%; cardiac death percentage of less than 15% for scores on BDI>/9; scores on BDI>/ 19 with a corresponding cardiac death percentage of less than 20% and scores on BDI>/ 19 with a corresponding cardiac death percentage of 30%. Thus, concluding that depression increases the risk of cardiac mortality by 1.6 times in cardiac patients.

In a study by Ariyo, Haan, Tangen et al. (2000), the purpose was to establish whether depressive symptoms constituted a risk for CHD and mortality among healthy Americans. A sample population of 5888 elderly Americans, among 65 years of age, enrolled in Cardiovascular Health Study(CHS). Out of which 4493 (80% whites and a 60 to 40 ratio of women to men) participants free of cardiovascular disease at baseline provided annual information on their depressive status, which was assessed using the Depression Scale of the Center for Epidemological Studies. These 4493 subjects were followed for 6 years for the development of CHD and mortality. The Wilcoxon-Mann-Whitney test was used for categorical covariates and the Spearman correlation for continuous covariates to assess the association between the covariate measures and the baseline depression scores. A multi-variant analysis adjusted for age, sex, education, diabetes mellitus, hypertension, smoking, cholesterol, triglyceride level, congestive heart failure, the hazard ratio obtained for depression to CHD was 1.15 times. The researchers of the study thus concluded that among elderly Americans, depressive symptoms constitute an independent risk factor for the development of CHD and mortality. Incremental risks associated with increasing levels of depressive scores were demonstrated.

Also, women reportedly suffer more than men from the adverse vascular effects of a depressive state; speculated due to the higher prevalence of depressive symptoms in women than men. Whooley, Jonge, Vittinghoff et al. (2008) in their study hypothesized that depressive symptoms predict adverse cardiovascular outcomes in patients with coronary heart disease. The sample population consisted of 1017 outpatients (2002), in San Francisco, with stable coronary heart disease with survival mean age of 4.8 years. All participants were made to go through electrocardiography to study the left ventricular function. The Patient Health Questionnaire (PHQ), a self-report instrument measuring the frequency of depressive symptoms corresponding to the DSM-IV, was administered. A standard cut-point of 10 or more was used to diagnose

minor depression. The presence of major depression was ascertained using the Computerized Diagnostic Interview Schedule for the DSM-IV. Out of the 1017 participants, 199 patients were diagnosed with having depressive symptoms (PHQ score >/ 10). Using the Cox Proportional Hazard Model, it was assessed that 341 cardiovascular events occurred during the 6-year follow-up. The age-adjusted annual rate of cardiovascular events was 10% among the 199 patients with depressive symptoms (PHQ score >/ 10) and 6.7% among the 818 participants without depressive symptoms (95% confidence interval). When the data was adjusted for age, physical activity and left ventricular function, increase in depressive symptom score was associated with a 15% greater risk of cardiovascular events. Thus, concluding that in the given sample population, of the outpatients with coronary heart disease, the association between depressive symptoms and adverse cardiovascular events was seen.

CONCLUSION: The objective of this review paper was to establish whether Depression is a precursor to Coronary Heart Disease or a resultant factor of it. For this purpose, original articles and review papers were analyzed in the context previous research done in the field of depression and coronary heart disease. As research shows it, the mechanism linking the relationship between depression and coronary heart disease is complex and multi-faceted. Thus, making it difficult to pin-point the bio-chemical and psychosocial factors influencing these variables. Through the process of putting together this paper, the author was able to gain an insight that depression and coronary heart disease share a significant relationship such that depression may precede the development of clinically evident CHD by years; and development depression may adverse cardiac mortality in a patient suffering from CHD, the absolute mechanisms, yet uncertain.

The studies conducted to study this phenomenon suffer from many drawbacks, which are discussed as follows:-

Firstly, Even though the majority of studies are longitudinal in nature, but the sample population is not representative in terms of a world population. The studies are concentrated in America and Europe and thus, do not take in account the socio-cultural variations, which affect the onset of depression and coronary heart disease, across regions and nations. Thus, the research obtained is low on external validity, that is, it cannot be generalized to the world population. The eating habits, sleeping habits, physical activity, social relations and variables like these differ across cultures and play an important role as a causative factor for both the diseases.

Secondly, there have been differences in the study structures, that is, inpatient vs. outpatient. Thus, making it difficult to ascertain the difference in the extent of depression in in-patients with coronary heart disease, in comparison to the extent of depression in outpatients with coronary disease. In other words, it difficult to assess whether there were signs and symptoms of depression before the patient was hospitalized or depression developed post hospitalization. This leads to the relationship between depression and coronary heart disease being categorized as uncertain and complex. Apart from being concentrated geographically, the sample size in most

of these studies is not large enough to be able to generalize the pattern of these variables in individuals. It varies from 32 to 5888. Still, some of the sample sizes are excessively small. This is a serious limitation because the nature of the normative sample determines the population it can be used for.

The sample population is not studied using in-depth information extracting tools, like case studies, which in themselves include various techniques of data collection, used together. The studies heavily rely on self-report measures for measuring the psychological disorder, depression. It is suggested that further research done in this field should include tools, which go beyond these self-report measures and hopefully give further insight in decoding and understanding the multi-faceted mechanisms for both depression and coronary heart disease. Also, this method would take into consideration the individual differences which may operate in the onset of these diseases across individuals. The methods thus used should be such that it makes it easier to find commonalities between the diseases, which are so diverse.

The limitations of self reporting measures are as follows :

- Social desirability: the tendency on the part of the respondent to endorse items in a socially desirable manner.
- Acquiescence: is the tendency to agree with items/questions irrespective of their contents, thus not providing a reliable estimate of the characteristic being measured.
- People may not have as much self-knowledge as the researchers assume
- Technically, they measure a perceptions of a construct rather than measuring it directly, and researchers must assume that this perception is an accurate enough reflection of the 'real' thing to be useful.

Other methods such as observations, projective techniques, behavioral analysis are useful too, each to an extent. Therefore, a combination, if possible should be used.

The research paper by Donoho, Stalls, Sydeman (2011), signified that not enough research has been done in Phase III and IV of Cardiac Rehabilitation (CR). One explanation of this was that since Phase III/IV demand expenses from the pocket of the patient and is not covered by the medical insurance, thus, majority of people hesitate in coming forward to participate in the same. Further research on similar lines must include phases III and IV as coronary heart disease is best studied in a longitudinal study structure, which includes all the phases of cardiac rehabilitation and not just limited to Phase II, which is an early stage. Also, across studies, the factors that are taken into consideration vary. For instance, a factor such as the age of the subject, which is seen to be an influencing factor for both depression and CHD, is not always given the importance it deserves. Another factor, in the same context is that studies pertaining to these variables are concentrated for the elderly population. The dizzying environmental changes have made

individuals at a much younger age, prone to these diseases. Thus, the sample population should not have a restricted range. Talking of restricted range, majority of the studies have sample populations which have a concentration of the white population. In this way, it is not taking into account the socio-cultural differences across different races.

From the gender perspective, research has shown that males are more prone to developing CHD whereas females are more prone to clinical depression. Again, adding complexity to the relationship between CHD and clinical depression. Adding a gender specific dimension can be speculative of some biological predispositions, pertaining to the neural wirings in both sexes. One major gap in the present scenario of research is that the majority of studies address the question of whether "Clinical depression leads to an increment in the cardiac mortality in a CHD patient?" or whether "Patients with CHD are at a greater risk of developing depression and increasing the chances of subsequent cardiac mortality. Extensive research needs to come up in the area addressing whether or not 'the onset of clinical depression can predict the development of CHD and subsequent cardiac mortality in the patient?'

On a concluding note, the research presented above offered new directions for further possible researches. But the aim of the research whether "depression is a precursor or a resultant factor of CHD" could not be met because of lack of evidence, both in terms the research not being exhaustive from the author's perspective and that previous research yet has not found a concrete mechanism pertaining to the relationship between clinical depression and coronary heart disease. Therefore, it can be assumed that only a more extensive research can enlighten us and throw us into new directions.